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Report to Congressional Requesters

December 2003

PRESCRIPTION DRUGS

OxyContin Abuse and Diversion and Efforts to Address the Problem

GAO-04-110

December 2003

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Highlights

Highlights of GAO-04-110, a report to congressional requesters

PRESCRIPTION DRUGS

OxyContin Abuse and Diversion and Efforts to Address the Problem

Why GAO Did This Study

Amid heightened awareness that many patients with cancer and other chronic diseases suffer from undertreated pain, the Food and Drug Administration (FDA) approved Purdue Pharma's controlled-release pain reliever OxyContin in 1995. Sales grew rapidly, and by 2001 OxyContin had become the most prescribed brand-name narcotic medication for treating moderate-to-severe pain. In early 2000, reports began to surface about abuse and diversion for illicit use of OxyContin, which contains the opioid oxycodone. GAO was asked to examine concerns about these issues. Specifically, GAO reviewed (1) how OxyContin was marketed and promoted, (2) what factors contributed to the abuse and diversion of OxyContin, and (3) what actions have been taken to address OxyContin abuse and diversion.

What GAO Recommends

To improve efforts to prevent or identify abuse and diversion of controlled substances such as OxyContin, FDA's risk management plan guidance should encourage pharmaceutical manufacturers with new drug applications to submit plans that contain a strategy for identifying potential problems with abuse and diversion. FDA concurred with GAO's recommendation. DEA agreed that such risk management plans are important, and Purdue stated that the report appeared to be fair and balanced.

www.gao.gov/cgi-bin/getrpt?GAO-04-110.

To view the full product, including the scope and methodology, click on the link above. For more information, contact Marcia Crosse at (202) 512-7119.

What GAO Found

Purdue conducted an extensive campaign to market and promote OxyContin using an expanded sales force to encourage physicians, including primary care specialists, to prescribe OxyContin not only for cancer pain but also as an initial opioid treatment for moderate-to-severe noncancer pain. OxyContin prescriptions, particularly those for noncancer pain, grew rapidly, and by 2003 nearly half of all OxyContin prescribers were primary care physicians. The Drug Enforcement Administration (DEA) has expressed concern that Purdue's aggressive marketing of OxyContin focused on promoting the drug to treat a wide range of conditions to physicians who may not have been adequately trained in pain management. FDA has taken two actions against Purdue for OxyContin advertising violations. Further, Purdue did not submit an OxyContin promotional video for FDA review upon its initial use in 1998, as required by FDA regulations.

Several factors may have contributed to the abuse and diversion of OxyContin. The active ingredient in OxyContin is twice as potent as morphine, which may have made it an attractive target for misuse. Further, the original label's safety warning advising patients not to crush the tablets because of the possible rapid release of a potentially toxic amount of oxycodone may have inadvertently alerted abusers to methods for abuse. Moreover, the significant increase in OxyContin's availability in the marketplace may have increased opportunities to obtain the drug illicitly in some states. Finally, the history of abuse and diversion of prescription drugs, including opioids, in some states may have predisposed certain areas to problems with OxyContin. However, GAO could not assess the relationship between the increased availability of OxyContin and locations of abuse and diversion because the data on abuse and diversion are not reliable, comprehensive, or timely.

Federal and state agencies and Purdue have taken actions to address the abuse and diversion of OxyContin. FDA approved a stronger safety warning on OxyContin's label. In addition, FDA and Purdue collaborated on a risk management plan to help detect and prevent OxyContin abuse and diversion, an approach that was not used at the time OxyContin was approved. FDA plans to provide guidance to the pharmaceutical industry by September 2004 on risk management plans, which are an optional feature of new drug applications. DEA has established a national action plan to prevent abuse and diversion of OxyContin. State agencies have investigated reports of abuse and diversion. In addition to developing a risk management plan, Purdue has initiated several OxyContin-related educational programs, taken disciplinary action against sales representatives who improperly promoted OxyContin, and referred physicians suspected of improper prescribing practices to the authorities.

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Abbreviations

DAWN	Drug Abuse Warning Network
DEA	Drug Enforcement Administration
FDA	Food and Drug Administration
FD&C Act	Federal Food, Drug and Cosmetic Act
HHS	Department of Health and Human Services
HIDTA	High Intensity Drug Trafficking Area
JCAHO	Joint Commission on Accreditation of Healthcare Organizations
NFLIS	National Forensic Laboratory Information System
ONDCP	Office of National Drug Control Policy
PDUFA	Prescription Drug User Fee Act of 1992
PhRMA	Pharmaceutical Research and Manufacturers of America
RADARS	Researched Abuse, Diversion, and Addiction-Related Surveillance
SAMHSA	Substance Abuse and Mental Health Services Administration
STRIDE	System to Retrieve Information from Drug Evidence
WHO	World Health Organization

United States General Accounting Office
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December 23, 2003

The Honorable Frank R. Wolf
Chairman
Subcommittee on Commerce, Justice, State, and the Judiciary,
and Related Agencies
Committee on Appropriations
House of Representatives

The Honorable James C. Greenwood
Chairman
Subcommittee on Oversight and Investigations
Committee on Energy and Commerce
House of Representatives

The Honorable Harold Rogers
House of Representatives

Patients with cancer may suffer from fairly constant pain for months or years. Patients with other diseases or conditions, such as rheumatoid arthritis, osteoarthritis, chronic back pain, or sickle cell anemia, may also suffer from pain that lasts for extended periods of time. Since 1986, the World Health Organization (WHO) and others have reported that the inadequate treatment of cancer and noncancer pain is a serious public health concern. To address this concern, efforts have been made to better educate health care professionals on the need to improve the treatment of both cancer and noncancer pain, including the appropriate role of prescription drugs.

Amid the heightened awareness that many people were suffering from undertreated pain, in 1995 the Food and Drug Administration (FDA) approved the new drug OxyContin, a controlled-release semisynthetic opioid analgesic manufactured by Purdue Pharma L.P.,[1] for the treatment of moderate-to-severe pain lasting more than a few days.[2] According to

[1]OxyContin is an opioid analgesic—a narcotic substance that relieves a person's pain without causing the loss of consciousness. Hereafter, we refer to the company as Purdue.

[2]As discussed later in this report, FDA approved the revised OxyContin label in July 2001 to describe the time frame as "when a continuous around-the-clock analgesic is needed for an extended period of time."

Purdue, OxyContin provides patients with continuous relief from pain over a 12-hour period, reduces pain fluctuations, requires fewer daily doses to help patients adhere to their prescribed regimen more easily, allows them to sleep through the night, and allows a physician to increase the OxyContin dose for a patient as needed to relieve pain.[3] Sales of the drug increased rapidly following its introduction to the marketplace in 1996. By 2001, sales had exceeded $1 billion annually, and OxyContin had become the most frequently prescribed brand-name narcotic medication for treating moderate-to-severe pain in the United States.

In early 2000, media reports began to surface in several states that OxyContin was being abused—that is, used for nontherapeutic purposes or for purposes other than those for which it was prescribed—and illegally diverted.[4] According to FDA and the Drug Enforcement Administration (DEA), the abuse of OxyContin is associated with serious consequences, including addiction, overdose, and death.[5] When OxyContin was approved, the federal government classified it as a schedule II controlled substance under the Controlled Substances Act because it has a high potential for abuse and may lead to severe psychological or physical dependence.[6] DEA has characterized the pharmacological effects of OxyContin, and its active ingredient oxycodone, as similar to those of heroin. Media reports indicated that abusers were crushing OxyContin tablets and snorting the powder or dissolving it in water and injecting it to defeat the intended controlled-release effect of the drug and attain a "rush" or "high" through

[3]According to FDA, there is no known limit to the amount of oxycodone, the active ingredient in OxyContin, that can be used to treat pain.

[4]Prescription drug diversion can involve such activities as "doctor shopping" by individuals who visit numerous physicians to obtain multiple prescriptions, prescription forgery, and pharmacy theft. Diversion can also involve illegal sales of prescription drugs by physicians, patients, or pharmacists, as well as obtaining controlled substances from Internet pharmacies without a valid prescription.

[5]According to the National Institute on Drug Abuse, addiction is a chronic, relapsing disease, characterized by compulsive drug seeking and use and by neurochemical and molecular changes in the brain, whereas physical dependence is an adaptive physiological state that can occur with regular drug use and results in withdrawal symptoms when drug use is discontinued.

[6]Under the Controlled Substances Act, which was enacted in 1970, drugs are classified as controlled substances and placed into one of five schedules based on their medicinal value, potential for abuse, and safety or dependence liability. Schedule I drugs have no medicinal value; have not been approved by FDA; and along with schedule II drugs, have the highest potential for abuse. Schedule II drugs have the highest potential for abuse of any approved drugs.

the body's rapid absorption of oxycodone. During a December 2001 congressional hearing, witnesses from DEA and other law enforcement officials from Kentucky, Virginia, and West Virginia described the growing problem of abuse and diversion of OxyContin.[7] Questions were raised about what factors may have caused the abuse and diversion, including whether Purdue's efforts to market the drug may have contributed to the problem. In February 2002, another congressional hearing was conducted on federal, state, and local efforts to decrease the abuse and diversion of OxyContin.[8]

Because of your concerns about these issues, you asked us to examine the marketing and promotion of OxyContin and its abuse and diversion. Specifically, we addressed the following questions:

1. How has Purdue marketed and promoted OxyContin?
2. What factors contributed to the abuse and diversion of OxyContin?
3. What actions have been taken to address OxyContin abuse and diversion?

To identify how Purdue marketed and promoted OxyContin, we interviewed Purdue officials and analyzed company documents and data. We also interviewed selected Purdue sales representatives who were high and midrange sales performers during 2001 and physicians who were among the highest prescribers of OxyContin. To determine how Purdue's marketing and promotion of OxyContin compared to that of other drugs, we examined the promotional materials and information related to FDA actions and interviewed officials from companies that manufacture and market three other opioid drugs, Avinza, Kadian, and Oramorph SR, that like OxyContin are classified as schedule II controlled substances.[9] Because of their concern about the proprietary nature of the information,

[7] *OxyContin*, Hearings of the Subcommittee on the Departments of Commerce, Justice, and State, the Judiciary, and Related Agencies, House Committee on Appropriations, 107th Cong. Part 10 (Dec. 11, 2001).

[8] *OxyContin: Balancing Risks and Benefits*, Hearing of the Senate Committee on Health, Education, Labor, and Pensions, 107th Cong. 287 (Feb. 12, 2002).

[9] Avinza was approved by FDA in 2002 and is marketed by Ligand Pharmaceuticals; Kadian was approved in 1996 and is marketed by Alpharma-US Human Pharmaceuticals; and Oramorph SR was approved in 1991 and is now owned by Élan Corporation, which told us it is not currently marketing the drug.

the three companies that market these drugs did not provide us with the same level of detail about the marketing and promotion of their drugs as did Purdue. We also examined data from DEA on promotional expenditures for OxyContin and two other schedule II controlled substances. To examine what factors may have contributed to the abuse and diversion of OxyContin, we interviewed officials from DEA, FDA, and Purdue and physicians who prescribe OxyContin. We also analyzed IMS Health data on sales of OxyContin nationwide and Purdue's distribution of sales representatives, as part of an effort to compare the areas with large sales growth and more sales representatives per capita with the areas where abuse and diversion problems were identified. However, limitations on the abuse and diversion data prevented an assessment of the relationship between the availability of OxyContin and areas where the drug was abused or diverted. To determine what actions have been taken to address OxyContin abuse and diversion, we interviewed FDA officials and examined FDA information regarding the drug's approval and marketing and promotion. We also interviewed DEA officials and examined how DEA determined the prevalence of OxyContin abuse and diversion nationally. In addition, we examined state efforts to identify those involved in the abuse and diversion of OxyContin. We also reviewed actions taken by Purdue to address this problem. (See app. I for a detailed discussion of our methodology.)

We performed our work from August 2002 through October 2003, in accordance with generally accepted government auditing standards.

Results in Brief

Purdue conducted an extensive campaign to market and promote OxyContin using an expanded sales force and multiple promotional approaches to encourage physicians, including primary care specialists, to prescribe OxyContin as an initial opioid treatment for noncancer pain. OxyContin sales and prescriptions grew rapidly following its market introduction in 1996, with the growth in prescriptions for noncancer pain outpacing the growth in prescriptions for cancer pain from 1997 through 2002. By 2003, nearly half of all OxyContin prescribers were primary care physicians. DEA has expressed concern that Purdue's aggressive marketing of OxyContin focused on promoting the drug to treat a wide range of conditions to physicians who may not have been adequately trained in pain management. Purdue has been cited twice by FDA for using potentially false or misleading medical journal advertisements for OxyContin that violated the Federal Food, Drug and Cosmetic Act (FD&C Act), including one advertisement that failed to include warnings about the potentially fatal risks associated with OxyContin use. Further, Purdue did

not submit an OxyContin promotional video for FDA review at the time of its initial distribution in 1998, as required by FDA regulations. Therefore, FDA did not have the opportunity to review the video at the time of its distribution to ensure that the information it contained was truthful, balanced, and accurately communicated. FDA reviewed a similar video in 2002 and told us that the video appeared to have made unsubstantiated claims about OxyContin and minimized its risks.

Several factors may have contributed to OxyContin's abuse and diversion. OxyContin's controlled-release formulation, which made the drug beneficial for the relief of moderate-to-severe pain over an extended period of time, enabled the drug to contain more of the active ingredient oxycodone than other, non-controlled-release oxycodone-containing drugs. This feature may have made OxyContin an attractive target for abuse and diversion, according to DEA. OxyContin's controlled-release formulation, which delayed the drug's absorption, also led FDA to include language in the original label stating that OxyContin had a lower potential for abuse than other oxycodone products. FDA officials thought that the controlled-release feature would make the drug less attractive to abusers. However, FDA did not recognize that the drug could be dissolved in water and injected, which disrupted the controlled-release characteristics and created an immediate rush or high, thereby increasing the potential for abuse. In addition, the safety warning on the label that advised patients not to crush the tablets because a rapid release of a potentially toxic amount of the drug could result—a customary precaution for controlled-release medications—may have inadvertently alerted abusers to a possible method for misusing the drug. The rapid growth in OxyContin sales, which increased the drug's availability in the marketplace, may have made it easier for abusers to obtain the drug for illicit purposes. Further, some geographic areas have been shown to have a history of prescription drug abuse and diversion that may have predisposed some states to the abuse and diversion of OxyContin. However, we could not assess the relationship between the increased availability of OxyContin and locations where it is being abused and diverted because the data on abuse and diversion are not reliable, comprehensive, or timely.

Since 2000, federal and state agencies and Purdue have taken several actions to try to address abuse and diversion of OxyContin. In July 2001, FDA approved a revised OxyContin label adding the highest level of safety warning that FDA can place on an approved drug product. The agency also collaborated with Purdue to develop and implement a risk management plan to help detect and prevent abuse and diversion of OxyContin. Risk management plans were not used at the time OxyContin was approved.

The plans are an optional feature of new drug applications that are intended to decrease product risks by using one or more interventions or tools beyond the approved product labeling. FDA plans to provide guidance on risk management plans to the pharmaceutical industry by September 2004. Also at the federal level, DEA initiated 257 OxyContin-related abuse and diversion cases in fiscal years 2001 and 2002, which resulted in 302 arrests and about $1 million in fines. At the state level, Medicaid fraud control units have investigated OxyContin abuse and diversion; however, they do not maintain precise data on the number of investigations and enforcement actions completed. Similarly, state medical licensure boards have investigated complaints about physicians who were suspected of abuse and diversion of controlled substances, but they could not provide data on the number of investigations involving OxyContin. Purdue has initiated education programs and other activities for physicians, pharmacists, and the public to address OxyContin abuse and diversion. Purdue has also taken disciplinary action against its sales representatives who improperly promoted OxyContin and has referred physicians who were suspected of misprescribing OxyContin to the appropriate authorities. Although Purdue has used very specific information on physician prescribing practices to market and promote OxyContin since its approval, it was not until October 2002 that Purdue began to use this information and other indicators to identify patterns of prescribing that could point to possible improper sales representative promotion or physician abuse and diversion of OxyContin.

To improve efforts to prevent or identify the abuse and diversion of schedule II controlled substances such as oxycodone, we recommend that FDA's risk management plan guidance encourage the pharmaceutical manufacturers that submit new drug applications for these substances to include plans that contain a strategy for monitoring the use of these drugs and identifying potential abuse and diversion problems.

We received comments on a draft of this report from FDA, DEA, and Purdue. FDA agreed with our recommendation that risk management plans for schedule II controlled substances contain a strategy for monitoring and identifying potential abuse and diversion problems. DEA reiterated its statement that Purdue's aggressive marketing of OxyContin exacerbated the abuse and diversion problems and noted that it is essential that risk management plans be put in place prior to the introduction of controlled substances into the marketplace. Purdue said the report appeared to be fair and balanced, but that we should add the media as one of the factors contributing to abuse and diversion problems

with OxyContin. We incorporated their technical comments where appropriate.

Background

Ensuring that pharmaceuticals are available for those with legitimate medical need while combating the abuse and diversion of prescription drugs involves the efforts of both federal and state government agencies. Under the FD&C Act, FDA is responsible for ensuring that drugs are safe and effective before they are available in the marketplace. The Controlled Substances Act,[10] which is administered by DEA, provides the legal framework for the federal government's oversight of the manufacture and wholesale distribution of controlled substances, that is, drugs and other chemicals that have a potential for abuse. The states address certain issues involving controlled substances through their own controlled substances acts and their regulation of the practice of medicine and pharmacy. In response to concerns about the influence of pharmaceutical marketing and promotional activities on physician prescribing practices, both the pharmaceutical industry and the Department of Health and Human Services's (HHS) Office of Inspector General have issued voluntary guidelines on appropriate marketing and promotion of prescription drugs.

Medical Treatment of Pain

As the incidence and prevalence of painful diseases have grown along with the aging of the population, there has been a growing acknowledgment of the importance of providing effective pain relief. Pain can be characterized in terms of intensity—mild to severe—and duration—acute (sudden onset) or chronic (long term). The appropriate medical treatment varies according to these two dimensions.

In 1986, WHO determined that cancer pain could be relieved in most if not all patients, and it encouraged physicians to prescribe opioid analgesics. WHO developed a three-step analgesic ladder as a practice guideline to provide a sequential use of different drugs for cancer pain management. For the first pain step, treatment with nonopioid analgesics, such as aspirin or ibuprofen, is recommended. If pain is not relieved, then an opioid such as codeine should be used for mild-to-moderate pain as the second step. For the third step—moderate-to-severe pain—opioids such as morphine should be used.

[10]Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970 (Pub. L. No. 91-513, §§100 et seq., 84 Stat. 1236, 1242 et seq.).

Beginning in the mid-1990s, various national pain-related organizations issued pain treatment and management guidelines, which included the use of opioid analgesics in treating both cancer and noncancer pain. In 1995, the American Pain Society recommended that pain should be treated as the fifth vital sign[11] to ensure that it would become common practice for health care providers to ask about pain when conducting patient evaluations. The practice guidelines issued by the Agency for Health Care Policy and Research provided physicians and other health care professionals with information on the management of acute pain in 1992 and cancer pain in 1994, respectively.[12] Health care providers and hospitals were further required to ensure that their patients received appropriate pain treatment when the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), a national health care facility standards-setting and accrediting body, implemented its pain standards for hospital accreditation in 2001.

OxyContin

OxyContin, a schedule II drug manufactured by Purdue Pharma L.P., was approved by FDA in 1995 for the treatment of moderate-to-severe pain lasting more than a few days, as indicated in the original label.[13] OxyContin followed Purdue's older product, MS Contin, a morphine-based product that was approved in 1984 for a similar intensity and duration of pain and during its early years of marketing was promoted for the treatment of cancer pain. The active ingredient in OxyContin tablets is oxycodone, a compound that is similar to morphine and is also found in oxycodone-combination pain relief drugs such as Percocet, Percodan, and Tylox. Because of its controlled-release property, OxyContin contains more active ingredient and needs to be taken less often (twice a day) than these

[11]The other four vital signs physicians use to assess patients are pulse, blood pressure, core temperature, and respiration.

[12]In 1999, the name of the Agency for Health Care Policy and Research was changed to the Agency for Healthcare Research and Quality. The agency, which is part of HHS, is responsible for supporting research designed to improve the quality of health care, reduce its costs, and broaden access to essential services.

[13]When we refer to OxyContin's label we are also referring to the drug's package insert that contains the same information about the product.

other oxycodone-containing drugs.[14] The OxyContin label originally approved by FDA indicated that the controlled-release characteristics of OxyContin were believed to reduce its potential for abuse. The label also contained a warning that OxyContin tablets were to be swallowed whole, and were not to be broken, chewed, or crushed because this could lead to the rapid release and absorption of a potentially toxic dose of oxycodone. Such a safety warning is customary for schedule II controlled-release medications. FDA first approved the marketing and use of OxyContin in 10-, 20-, and 40-milligram controlled-release tablets. FDA later approved 80- and 160-milligram controlled-release tablets for use by patients who were already taking opioids.[15] In July 2001, FDA approved the revised label to state that the drug is approved for the treatment of moderate-to-severe pain in patients who require "a continuous around-the-clock analgesic for an extended period of time." (See app. II for a summary of the changes that were made by FDA to the original OxyContin label.)

OxyContin sales and prescriptions grew rapidly following its market introduction in 1996. Fortuitous timing may have contributed to this growth, as the launching of the drug occurred during the national focus on the inadequacy of patient pain treatment and management. In 1997, OxyContin's sales and prescriptions began increasing significantly, and they continued to increase through 2002. In both 2001 and 2002, OxyContin's sales exceeded $1 billion, and prescriptions were over 7 million. The drug became Purdue's main product, accounting for 90 percent of the company's total prescription sales by 2001.

Media reports of OxyContin abuse and diversion began to surface in 2000. These reports first appeared in rural areas of some states, generally in the Appalachian region, and continued to spread to other rural areas and larger cities in several states. Rural communities in Maine, Kentucky, Ohio, Pennsylvania, Virginia, and West Virginia were reportedly being devastated by the abuse and diversion of OxyContin. For example, media reports told of persons and communities that had been adversely affected by the rise of addiction and deaths related to OxyContin. One report noted that drug

[14]For example, according to Purdue's comparable dose guide a patient taking one Percodan 4.5-milligram tablet or one Tylox 5-milligram tablet every 6 hours can be converted to either a 10- or a 20-milligram OxyContin tablet to be taken every 12 hours. For a 12-hour dosing period, one OxyContin tablet replaces two Percodan or Tylox tablets, and one OxyContin tablet contains twice as much oxycodone as one of the other tablets.

[15]In April 2001, Purdue discontinued distribution of the 160-milligram tablets because of OxyContin abuse and diversion concerns.

treatment centers and emergency rooms in a particular area were receiving new patients who were addicted to OxyContin as early as 1999. Pain patients, teens, and recreational drug users who had abused OxyContin reportedly entered drug treatment centers sweating and vomiting from withdrawal. In West Virginia, as many as one-half of the approximately 300 patients admitted to a drug treatment clinic in 2000 were treated for OxyContin addiction. The media also reported on deaths due to OxyContin. For example, a newspaper's investigation of autopsy reports involving oxycodone-related deaths found that OxyContin had been involved in over 200 overdose deaths in Florida since 2000.[16] In another case, a forensic toxicologist commented that he had reviewed a number of fatal overdose cases in which individuals took a large dose of OxyContin, in combination with alcohol or other drugs.

After learning about the initial reports of abuse and diversion of OxyContin in Maine in 2000, Purdue formed a response team made up of its top executives and physicians to initiate meetings with federal and state officials in Maine to gain an understanding of the scope of the problem and to devise strategies for preventing abuse and diversion. After these meetings, Purdue distributed brochures to health care professionals that described several steps that could be taken to prevent prescription drug abuse and diversion. In response to the abuse and diversion reports, DEA analyzed data collected from medical examiner autopsy reports and crime scene investigation reports. The most recent data available from DEA show that as of February 2002, the agency had verified 146 deaths nationally involving OxyContin in 2000 and 2001.

According to Purdue, as of early October 2003, over 300 lawsuits concerning OxyContin were pending against Purdue, and 50 additional lawsuits had been dismissed. The cases involve many allegations, including, for example, that Purdue used improper sales tactics and overpromoted OxyContin causing the drug to be inappropriately prescribed by physicians, and that Purdue took inadequate actions to prevent addiction, abuse, and diversion of the drug. The lawsuits have been brought in 25 states and the District of Columbia in both federal and state courts.

[16]Doris Bloodsworth, "Pain Pill Leaves Death Trail: A Nine-Month Investigation Raises Many Questions about Purdue Pharma's Powerful Drug OxyContin," *Orlando Sentinel*, Oct. 19, 2003.

Controlled Substances Act

The Controlled Substances Act established a classification structure for drugs and chemicals used in the manufacture of drugs that are designated as controlled substances.[17] Controlled substances are classified by DEA into five schedules on the basis of their medicinal value, potential for abuse, and safety or dependence liability. Schedule I drugs—including heroin, marijuana, and LSD—have a high potential for abuse and no currently accepted medical use. Schedule II drugs—which include opioids such as morphine and oxycodone, the primary ingredient in OxyContin—have a high potential for abuse among drugs with an accepted medical use and may lead to severe psychological or physical dependence. Drugs on schedules III through V have medical uses and successively lower potentials for abuse and dependence. Schedule III drugs include anabolic steroids, codeine, hydrocodone in combination with aspirin or acetaminophen, and some barbiturates. Schedule IV contains such drugs as the antianxiety drugs diazepam (Valium) and alprazolam (Xanax). Schedule V includes preparations such as cough syrups with codeine. All scheduled drugs except those in schedule I are legally available to the public with a prescription.[18]

FDA's Regulation of Prescription Drugs

Under the FD&C Act and implementing regulations, FDA is responsible for ensuring that all new drugs are safe and effective. FDA reviews scientific and clinical data to decide whether to approve drugs based on their intended use, effectiveness, and the risks and benefits for the intended population, and also monitors drugs for continued safety after they are in use.

FDA also regulates the advertising and promotion of prescription drugs under the FD&C Act. FDA carries out this responsibility by ensuring that prescription drug advertising and promotion is truthful, balanced, and accurately communicated.[19] The FD&C Act makes no distinction between

[17]Section 201, classified to 21 U.S.C. § 811.

[18]Some schedule V drugs that contain limited quantities of certain narcotic and stimulant drugs are available over the counter, without a prescription.

[19]FDA regulations require that promotional labeling and advertisements be submitted to FDA at the time of initial dissemination (for labeling) and initial publication (for advertisements). The FD&C Act defines labeling to include all labels and other written, printed, or graphic matter accompanying an article. For example, promotional materials commonly shown or given to physicians, such as sales aids and branded promotional items, are regulated as promotional labeling. FDA may also regulate promotion by sales representatives on computer programs, through fax machines, or on electronic bulletin boards.

controlled substances and other prescription drugs in the oversight of promotional activities. FDA told us that the agency takes a risk-based approach to enforcement, whereby drugs with more serious risks, such as opioids, are given closer scrutiny in monitoring promotional messages and activities, but the agency has no specific guidance or policy on this approach. The FD&C Act and its implementing regulations require that all promotional materials for prescription drugs be submitted to FDA at the time the materials are first disseminated or used, but it generally is not required that these materials be approved by FDA before their use. As a result, FDA's actions to address violations occur after the materials have already appeared in public. In fiscal year 2002, FDA had 39 staff positions dedicated to oversight of drug advertising and promotion of all pharmaceuticals distributed in the United States. According to FDA, most of the staff focuses on the oversight of promotional communications to physicians. FDA officials told us that in 2001 it received approximately 34,000 pieces of promotional material, including consumer advertisements and promotions to physicians, and received and reviewed 230 complaints about allegedly misleading advertisements, including materials directed at health professionals.[20]

FDA issues two types of letters to address violations of the FD&C Act: untitled letters and warning letters. Untitled letters are issued for violations such as overstating the effectiveness of the drug, suggesting a broader range of indicated uses than the drug has been approved for, and making misleading claims because of inadequate context or lack of balanced information. Warning letters are issued for more serious violations, such as those involving safety or health risks, or for continued violations of the act. Warning letters generally advise a pharmaceutical manufacturer that FDA may take further enforcement actions, such as seeking judicial remediation, without notifying the company and may ask the manufacturer to conduct a new advertising campaign to correct inaccurate impressions left by the advertisements.

Under the Controlled Substances Act, FDA notifies DEA if FDA is reviewing a new drug application for a drug that has a stimulant, depressant, or hallucinogenic effect on the central nervous system and has abuse potential. FDA performs a medical and scientific assessment as

[20]For details on FDA's oversight of drug advertising see U.S. General Accounting Office, *Prescription Drugs: FDA Oversight of Direct-to-Consumer Advertising Has Limitations*, GAO-03-177 (Washington, D.C.: Oct. 28, 2002).

required by the Controlled Substances Act, and recommends to DEA an initial schedule level to be assigned to a new controlled substance.

FDA plans to provide guidance to the pharmaceutical industry on the development, implementation, and evaluation of risk management plans as a result of the reauthorization of the Prescription Drug User Fee Act of 1992 (PDUFA).[21] FDA expects to issue this guidance by September 30, 2004. FDA defines a risk management program as a strategic safety program that is designed to decrease product risks by using one or more interventions or tools beyond the approved product labeling. Interventions used in risk management plans may include postmarketing surveillance, education and outreach programs to health professionals or consumers, informed consent agreements for patients, limitations on the supply or refills of products, and restrictions on individuals who may prescribe and dispense drug products. All drug manufacturers have the option to develop and submit risk management plans to FDA as part of their new drug applications.

DEA's Regulation of Controlled Substances

DEA is the primary federal agency responsible for enforcing the Controlled Substances Act. DEA has the authority to regulate transactions involving the sale and distribution of controlled substances at the manufacturer and wholesale distributor levels. DEA registers legitimate handlers of controlled substances—including manufacturers, distributors, hospitals, pharmacies, practitioners, and researchers—who must comply with regulations relating to drug security and accountability through the maintenance of inventories and records. All registrants, including pharmacies, are required to maintain records of controlled substances that have been manufactured, purchased, and sold. Manufacturers and distributors are also required to report their annual inventories of controlled substances to DEA. The data provided to DEA are available for use in monitoring the distribution of controlled substances throughout the United States and identifying retail-level registrants that received unusual quantities of controlled substances. DEA regulations for schedule II prescription drugs, unlike those for other prescription drugs, require that each prescription must be written and signed by the physician and may not be telephoned in to the pharmacy except in an emergency. Also, a

[21]The Prescription Drug User Fee Act of 1992, Pub. L. No. 102-571, title I, 106 Stat. 4491, was reauthorized by the Food and Drug Modernization Act of 1997, Pub. L. No. 105-115, 111 Stat. 2296, and, most recently, by the Prescription Drug User Fee Amendments of 2002, Pub. L. No. 107-188, title V, subtitle A, 116 Stat. 594, 687.

prescription for a schedule II drug may not be refilled. A physician is required to provide a new prescription each time a patient obtains more of the drug. DEA also sets limits on the quantity of schedule II controlled substances that may be produced in the United States in any given year. Specifically, DEA sets aggregate production quotas that limit the production of bulk raw materials used in the manufacture of controlled substances. DEA determines these quotas based on a variety of data including sales, production, inventories, and exports. Individual companies must apply to DEA for manufacturing or procurement quotas for specific pharmaceutical products. For example, Purdue has a procurement quota for oxycodone, the principle ingredient in OxyContin, that allows the company to purchase specified quantities of oxycodone from bulk manufacturers.

States' Regulation of the Practice of Medicine and Pharmacy and Role in Monitoring Illegal Use and Diversion of Prescription Drugs

State laws govern the prescribing and dispensing of prescription drugs by licensed health care professionals. Each state requires that physicians practicing in the state be licensed, and state medical practice laws generally outline standards for the practice of medicine and delegate the responsibility of regulating physicians to state medical boards. States also require pharmacists and pharmacies to be licensed. The regulation of the practice of pharmacy is based on state pharmacy practice acts and regulations enforced by the state boards of pharmacy. According to the National Association of Boards of Pharmacy, all state pharmacy laws require that records of prescription drugs dispensed to patients be maintained and that state pharmacy boards have access to the prescription records. State regulatory boards face new challenges with the advent of Internet pharmacies, because they enable pharmacies and physicians to anonymously reach across state borders to prescribe, sell, and dispense prescription drugs without complying with state requirements.[22] In some cases, consumers can purchase prescription drugs, including controlled substances, such as OxyContin, from Internet pharmacies without a valid prescription.

[22]For more details on Internet pharmacies, see U.S. General Accounting Office, *Internet Pharmacies: Adding Disclosure Requirements Would Aid State and Federal Oversight*, GAO-01-69 (Washington, D.C.: Oct. 19, 2000).

In addition to these regulatory boards, 15 states operate prescription drug monitoring programs as a means to control the illegal diversion of prescription drugs that are controlled substances. Prescription drug monitoring programs are designed to facilitate the collection, analysis, and reporting of information on the prescribing, dispensing, and use of controlled substances within a state. They provide data and analysis to state law enforcement and regulatory agencies to assist in identifying and investigating activities potentially related to the illegal prescribing, dispensing, and procuring of controlled substances. For example, physicians in Kentucky can use the program to check a patient's prescription drug history to determine if the individual may be "doctor shopping" to seek multiple controlled substance prescriptions. An overriding goal of prescription drug monitoring programs is to support both the state laws ensuring access to appropriate pharmaceutical care by citizens and the state laws deterring diversion. As we have reported, state prescription drug monitoring programs offer state regulators an efficient means of detecting and deterring illegal diversion. However, few states proactively analyze prescription data to identify individuals, physicians, or pharmacies that have unusual use, prescribing, or dispensing patterns that may suggest potential drug diversion or abuse. Although three states can respond to requests for information within 3 to 4 hours, providing information on suspected illegal prescribing, dispensing, or doctor shopping at the time a prescription is written or sold would require states to improve computer capabilities. In addition, state prescription drug monitoring programs may require additional legal authority to analyze data proactively.[23]

Guidelines for Marketing Drugs to Health Care Professionals

At the time that OxyContin was first marketed, there were no industry or federal guidelines for the promotion of prescription drugs. Voluntary guidelines regarding how drug companies should market and promote their drugs to health care professionals were issued in July 2002 by the Pharmaceutical Research and Manufacturers of America (PhRMA). In April 2003, HHS's Office of Inspector General issued voluntary guidelines for how drug companies should market and promote their products to federal health care programs. Neither set of guidelines distinguishes between controlled and noncontrolled substances.

[23]For more details on these programs, see U.S. General Accounting Office, *Prescription Drugs: State Monitoring Programs Provide Useful Tool to Reduce Diversion*, GAO-02-634 (Washington, D.C.: May 17, 2002).

PhRMA's voluntary code of conduct for sales representatives states that interactions with health care professionals should be to inform these professionals about products, to provide scientific and educational information, and to support medical research and education.[24] The question-and-answer section of the code addresses companies' use of branded promotional items, stating, for example, that golf balls and sports bags should not be distributed because they are not primarily for the benefit of patients, but that speaker training programs held at golf resorts may be acceptable if participants are receiving extensive training. Purdue adopted the code.

In April 2003, HHS's Office of Inspector General issued final voluntary guidance for drug companies' interactions with health care professionals in connection with federal health care programs, including Medicare and Medicaid. Among the guidelines were cautions for companies against offering inappropriate travel, meals, and gifts to influence the prescribing of drugs; making excessive payments to physicians for consulting and research services; and paying physicians to switch their patients from competitors' drugs.

Purdue Conducted an Extensive Campaign to Market and Promote OxyContin

Purdue conducted an extensive campaign to market and promote OxyContin that focused on encouraging physicians, including those in primary care specialties, to prescribe the drug for noncancer as well as cancer pain. To implement its OxyContin campaign, Purdue significantly increased its sales force and used multiple promotional approaches. OxyContin sales and prescriptions grew rapidly following its market introduction, with the growth in prescriptions for noncancer pain outpacing the growth in prescriptions for cancer pain. DEA has expressed concern that Purdue marketed OxyContin for a wide variety of conditions to physicians who may not have been adequately trained in pain management. Purdue has been cited twice by FDA for OxyContin advertisements in medical journals that violated the FD&C Act. FDA has also taken similar actions against manufacturers of two of the three comparable schedule II controlled substances we examined, to ensure that

[24]In addition, the American Medical Association, a professional association for physicians, issued guidelines in 1990 regarding gifts given to physicians by drug industry representatives. For example, physicians may accept individual gifts of nominal value that are related to their work, such as notepads and pens, and may attend conferences sponsored by drug companies that are educational and for which appropriate disclosure of financial support or conflicts of interest is made.

their marketing and promotion were truthful, balanced, and accurately communicated. In addition, Purdue provided two promotional videos to physicians that, according to FDA appear to have made unsubstantiated claims and minimized the risks of OxyContin. The first video was available for about 3 years without being submitted to FDA for review.

Purdue Focused on Promoting OxyContin for Treatment of Noncancer Pain

From the outset of the OxyContin marketing campaign, Purdue promoted the drug to physicians for noncancer pain conditions that can be caused by arthritis, injuries, and chronic diseases, in addition to cancer pain. Purdue directed its sales representatives to focus on the physicians in their sales territories who were high opioid prescribers. This group included cancer and pain specialists, primary care physicians, and physicians who were high prescribers of Purdue's older product, MS Contin. One of Purdue's goals was to identify primary care physicians who would expand the company's OxyContin prescribing base. Sales representatives were also directed to call on oncology nurses, consultant pharmacists, hospices, hospitals, and nursing homes.

From OxyContin's launch until its July 2001 label change, Purdue used two key promotional messages for primary care physicians and other high prescribers. The first was that physicians should prescribe OxyContin for their pain patients both as the drug "to start with and to stay with." The second contrasted dosing with other opioid pain relievers with OxyContin dosing as "the hard way versus the easy way" to dose because OxyContin's twice-a-day dosing was more convenient for patients.[25] Purdue's sales representatives promoted OxyContin to physicians as an initial opioid treatment for moderate-to-severe pain lasting more than a few days, to be prescribed instead of other single-entity opioid analgesics or short-acting combination opioid pain relievers. Purdue has stated that by 2003 primary care physicians had grown to constitute nearly half of all OxyContin prescribers, based on data from IMS Health, an information service providing pharmaceutical market research. DEA's analysis of physicians prescribing OxyContin found that the scope of medical specialties was wider for OxyContin than five other controlled-release, schedule II narcotic analgesics. DEA expressed concern that this resulted in

[25]Following OxyContin's July 2001 label change, Purdue modified its promotional messages but continued to focus on encouraging physicians to prescribe OxyContin for patients taking pain relievers every 4 to 6 hours. In 2003, Purdue began using the promotional claim "there can be life with relief" in OxyContin promotion.

OxyContin's being promoted to physicians who were not adequately trained in pain management.

Purdue's promotion of OxyContin for the treatment of noncancer pain contributed to a greater increase in prescriptions for noncancer pain than for cancer pain from 1997 through 2002.[26] According to IMS Health data, the annual number of OxyContin prescriptions for noncancer pain increased nearly tenfold, from about 670,000 in 1997 to about 6.2 million in 2002.[27] In contrast, during the same 6 years, the annual number of OxyContin prescriptions for cancer pain increased about fourfold, from about 250,000 in 1997 to just over 1 million in 2002. The noncancer prescriptions therefore increased from about 73 percent of total OxyContin prescriptions to about 85 percent during that period, while the cancer prescriptions decreased from about 27 percent of the total to about 15 percent. IMS Health data indicated that prescriptions for other schedule II opioid drugs, such as Duragesic[28] and morphine products, for noncancer pain also increased during this period. Duragesic prescriptions for noncancer pain were about 46 percent of its total prescriptions in 1997, and increased to about 72 percent of its total in 2002. Morphine products, including, for example, Purdue's MS Contin, also experienced an increase in their noncancer prescriptions during the same period. Their noncancer prescriptions were about 42 percent of total prescriptions in 1997, and increased to about 65 percent in 2002. DEA has cited Purdue's focus on promoting OxyContin for treating a wide range of conditions as one of the reasons the agency considered Purdue's marketing of OxyContin to be overly aggressive.

[26]IMS Health reported noncancer prescriptions written for the following types of pain conditions: surgical aftercare; musculoskeletal disorders including back and neck disorders, arthritis conditions, and injuries and trauma including bone fractures; central nervous system disorders including headache conditions such as migraines; genitourinary disorders including kidney stones; and other types of general pain.

[27]The IMS Health data included information from the National Disease and Therapeutics Index and the National Prescription Audit. The National Disease and Therapeutics Index does not capture data from anesthesiologists and dental specialties. The National Prescription Audit data include retail pharmacy, long-term-care, and mail-order prescriptions.

[28]Duragesic is a skin patch used to deliver the opioid pain reliever fentanyl over a 72-hour period.

Purdue Significantly Increased Its Sales Force to Market and Promote OxyContin

Purdue significantly increased its sales force to market and promote OxyContin to physicians and other health care practitioners. In 1996, Purdue began promoting OxyContin with a sales force of approximately 300 representatives in its Prescription Sales Division.[29] Through a 1996 copromotion agreement, Abbott Laboratories provided at least another 300 representatives, doubling the total OxyContin sales force.[30] By 2000, Purdue had more than doubled its own internal sales force to 671. The expanded sales force included sales representatives from the Hospital Specialty Division, which was created in 2000 to increase promotional visits on physicians located in hospitals. (See table 1.)

Table 1: Sales Representative Positions Available for OxyContin Promotion, 1996 through 2002

Positions available[a]	1996	1997	1998	1999	2000	2001	2002
Purdue Prescription Sales Division	318	319	377	471	562	641	641
Purdue Hospital Specialty Division	0	0	0	0	109	125	126
Subtotal—All Purdue sales representatives	**318**	**319**	**377**	**471**	**671**	**766**	**767**
Abbott Laboratories sales representatives[b]	300	300	300	300	300	300	300
Total	**618**	**619**	**677**	**771**	**971**	**1,066**	**1,067**

Source: GAO analysis of Purdue data.

[a]All positions were not necessarily filled in a given year.

[b]Under the OxyContin copromotion agreement, Abbott Laboratories provided at least 300 sales representatives each year.

The manufacturers of two of the three comparable schedule II drugs have smaller sales forces than Purdue. Currently, the manufacturer of Kadian has about 100 sales representatives and is considering entering into a copromotion agreement. Elan, the current owner of Oramorph SR, has approximately 300 representatives, but told us that it is not currently marketing Oramorph SR. The manufacturer of Avinza had approximately 50 representatives at its product launch. In early 2003, Avinza's manufacturer announced that more than 700 additional sales

[29]These sales representatives were also responsible for promoting other Purdue products.

[30]Abbott Laboratories sales representatives' promotion of OxyContin is limited to hospital-based anesthesiologists and surgeons and major hospitals, medical centers, and freestanding pain clinics.

representatives would be promoting the drug under its copromotion agreement with the pharmaceutical manufacturer Organon—for a total of more than 800 representatives.

By more than doubling its total sales representatives, Purdue significantly increased the number of physicians to whom it was promoting OxyContin. Each Purdue sales representative has a specific sales territory and is responsible for developing a list of about 105 to 140 physicians to call on who already prescribe opioids or who are candidates for prescribing opioids. In 1996, the 300-plus Purdue sales representatives had a total physician call list of approximately 33,400 to 44,500. By 2000, the nearly 700 representatives had a total call list of approximately 70,500 to 94,000 physicians. Each Purdue sales representative is expected to make about 35 physician calls per week and typically calls on each physician every 3 to 4 weeks. Each hospital sales representative is expected to make about 50 calls per week and typically calls on each facility every 4 weeks.

Purdue stated it offered a "better than industry average" salary and sales bonuses to attract top sales representatives and provide incentives to boost OxyContin sales as it had done for MS Contin. Although the sales representatives were primarily focused on OxyContin promotion, the amount of the bonus depended on whether a representative met the sales quotas in his or her sales territory for all company products. As OxyContin's sales increased, Purdue's growth-based portion of the bonus formula increased the OxyContin sales quotas necessary to earn the same base sales bonus amounts. The amount of total bonuses that Purdue estimated were tied to OxyContin sales increased significantly from about $1 million in 1996, when OxyContin was first marketed, to about $40 million in 2001. Beginning in 2000, when the newly created hospital specialty representatives began promoting OxyContin, their estimated total bonuses were approximately $6 million annually. In 2001, the average annual salary for a Purdue sales representative was $55,000, and the average annual bonus was $71,500. During the same year, the highest annual sales bonus was nearly $240,000, and the lowest was nearly $15,000. In 2001, Purdue decided to limit the sales bonus a representative could earn based on the growth in prescribing of a single physician after a meeting with the U.S. Attorney for the Western District of Virginia at which the company was informed of the possibility that a bonus could be based on the prescribing of one physician.

Purdue Employed Multiple Approaches to Market and Promote OxyContin

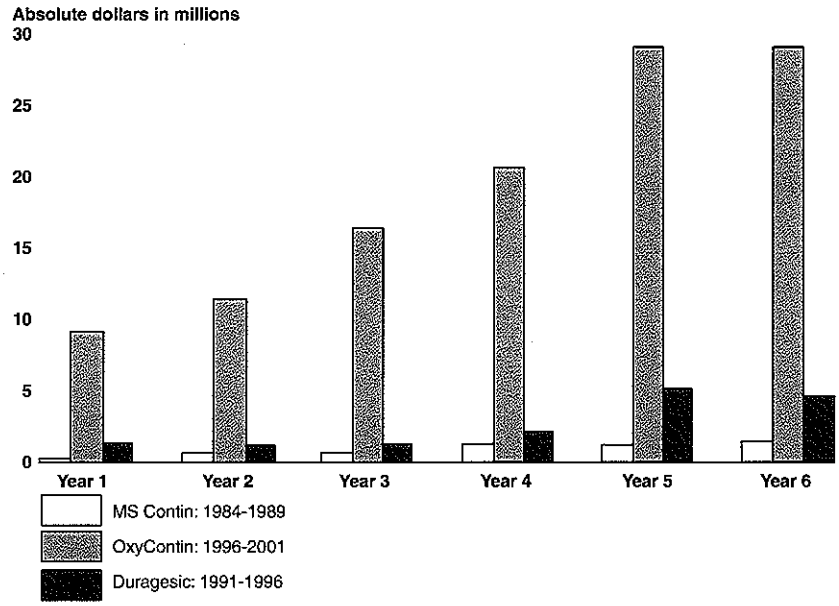
In addition to expanding its sales force, Purdue used multiple approaches to market and promote OxyContin. These approaches included expanding its physician speaker bureau and conducting speaker training conferences, sponsoring pain-related educational programs, issuing OxyContin starter coupons for patients' initial prescriptions, sponsoring pain-related Web sites, advertising OxyContin in medical journals, and distributing OxyContin marketing items to health care professionals.

In our report on direct-to-consumer advertising, we found that most promotional spending is targeted to physicians.[31] For example, in 2001, 29 percent of spending on pharmaceutical promotional activities was related to activities of pharmaceutical sales representatives directed to physicians, and 2 percent was for journal advertising—both activities Purdue uses for its OxyContin promotion. The remaining 69 percent of pharmaceutical promotional spending involved sampling (55 percent), which is the practice of providing drug samples during sales visits to physician offices, and direct-to-consumer advertising (14 percent)—both activities that Purdue has stated it does not use for OxyContin.

According to DEA's analysis of IMS Health data, Purdue spent approximately 6 to 12 times more on promotional efforts during OxyContin's first 6 years on the market than it had spent on its older product, MS Contin, during its first 6 years, or than had been spent by Janssen Pharmaceutical Products, L.P., for one of OxyContin's drug competitors, Duragesic. (See fig. 1.)

[31]U.S. General Accounting Office, *Prescription Drugs: FDA Oversight of Direct-to-Consumer Advertising Has Limitations*, GAO-03-177 (Washington, D.C.: Oct. 28, 2002).

Figure 1: Promotional Spending for Three Opioid Analgesics in First 6 Years of Sales



Source: DEA and IMS Health, Integrated Promotional Service Audit.

Note: Dollars are 2002 adjusted.

During the first 5 years that OxyContin was marketed, Purdue conducted over 40 national pain management and speaker training conferences, usually in resort locations such as Boca Raton, Florida, and Scottsdale, Arizona, to recruit and train health care practitioners for its national speaker bureau. The trained speakers were then made available to speak about the appropriate use of opioids, including oxycodone, the active ingredient in OxyContin, to their colleagues in various settings, such as local medical conferences and grand round presentations in hospitals involving physicians, residents, and interns. Over the 5 years, these conferences were attended by more than 5,000 physicians, pharmacists, and nurses, whose travel, lodging, and meal costs were paid by the company. Purdue told us that less than 1 percent annually of the physicians called on by Purdue sales representatives attended these conferences. Purdue told us it discontinued conducting these conferences in fall 2000. Purdue's speaker bureau list from 1996 through mid-2002 included nearly 2,500 physicians, of whom over 1,000 were active participants. Purdue has paid participants a fee for speaking based on the physician's qualifications; the type of program and time commitment

involved; and expenses such as airfare, hotel, and food. The company currently marketing the comparable drug Avinza has a physician speaker bureau, but does not sponsor speaker training and conferences at resort locations. Kadian's current company does not have a physician speaker bureau and has not held any conferences.

From 1996, when OxyContin was introduced to the market, to July 2002, Purdue has funded over 20,000 pain-related educational programs through direct sponsorship or financial grants. These grants included support for programs to provide physicians with opportunities to earn required continuing medical education credits, such as grand round presentations at hospitals and medical education seminars at state and local medical conferences. During 2001 and 2002, Purdue funded a series of nine programs throughout the country to educate hospital physicians and staff on how to comply with JCAHO's pain standards for hospitals and to discuss postoperative pain treatment. Purdue was one of only two drug companies that provided funding for JCAHO's pain management educational programs.[32] Under an agreement with JCAHO, Purdue was the only drug company allowed to distribute certain educational videos and a book about pain management; these materials were also available for purchase from JCAHO's Web site. Purdue's participation in these activities with JCAHO may have facilitated its access to hospitals to promote OxyContin.

For the first time in marketing any of its products, Purdue used a patient starter coupon program for OxyContin to provide patients with a free limited-time prescription. Unlike patient assistance programs, which provide free prescriptions to patients in financial need, a coupon program is intended to enable a patient to try a new drug through a one-time free prescription. A sales representative distributes coupons to a physician, who decides whether to offer one to a patient, and then the patient redeems it for a free prescription through a participating pharmacy. The program began in 1998 and ran intermittently for 4 years. In 1998 and 1999, each sales representative had 25 coupons that were redeemable for a free 30-day supply. In 2000 each representative had 90 coupons for a 7-day supply, and in 2001 each had 10 coupons for a 7-day supply. Approximately 34,000 coupons had been redeemed nationally when the

[32]During 2000 through 2002, JCAHO sponsored a series of educational programs on pain management standards with various cosponsors, including pain-related groups such as the American Pain Society and the American Academy of Pain Medicine.

program was terminated following the July 2001 OxyContin label change. The manufacturers of two of the comparable drugs we examined—Avinza and Kadian—used coupon programs to introduce patients to their products. Avinza's coupon program requires patients to make a copayment to cover part of the drug's cost.

Purdue has also used Web sites to provide pain-related information to consumers and others. In addition to its corporate Web site, which provides product information, Purdue established the "Partners Against Pain" Web site in 1997 to provide consumers with information about pain management and pain treatment options. According to FDA, the Web site also contained information about OxyContin. Separate sections provide information for patients and caregivers, medical professionals, and institutions. The Web site includes a "Find a Doctor" feature to enable consumers to find physicians who treat pain in their geographic area.[33] As of July 2002, over 33,000 physicians were included. Ligand, which markets Avinza, one of the comparable drugs, has also used a corporate Web site to provide product information. Purdue has also funded Web sites, such as FamilyPractice.com, that provide physicians with free continuing medical educational programs on pain management.[34] Purdue has also provided funding for Web site development and support for health care groups such as the American Chronic Pain Association and the American Academy of Pain Medicine. In addition, Purdue is one of 28 corporate donors—which include all three comparable drug companies—listed on the Web site of the American Pain Society, the mission of which is to improve pain-related education, treatment, and professional practice. Purdue also sponsors painfullyobvious.com, which it describes as a youth-focused "message campaign designed to provide information—and stimulate open discussions—on the dangers of abusing prescription drugs."

Purdue also provided its sales representatives with 14,000 copies of a promotional video in 1999 to distribute to physicians. Entitled *From One Pain Patient to Another: Advice from Patients Who Have Found Relief*, the video was to encourage patients to report their pain and to alleviate patients' concerns about taking opioids. Purdue stated that the video was to be used "in physician waiting rooms, as a 'check out' item for an office's

[33]The "Find a Doctor" feature is a physician listing service provided by the National Physicians DataSource, LLC.

[34]Purdue has also helped to fund the Dannemiller Memorial Education Foundation and the American Academy of Physician Assistants Web sites.

patient education library, or as an educational tool for office or hospital staff to utilize with patients and their families." Copies of the video were also available for ordering on the "Partners Against Pain" Web site from June 2000 through July 2001. The video did not need to be submitted to FDA for its review because it did not contain any information about OxyContin. However, the video included a statement that opioid analgesics have been shown to cause addiction in less than 1 percent of patients. According to FDA, this statement has not been substantiated.

As part of its marketing campaign, Purdue distributed several types of branded promotional items to health care practitioners. Among these items were OxyContin fishing hats, stuffed plush toys, coffee mugs with heat-activated messages, music compact discs, luggage tags, and pens containing a pullout conversion chart showing physicians how to calculate the dosage to convert a patient to OxyContin from other opioid pain relievers.[35] In May 2002, in anticipation of PhRMA's voluntary guidance for sales representatives' interactions with health care professionals, Purdue instructed its sales force to destroy any remaining inventory of non-health-related promotional items, such as stuffed toys or golf balls. In early 2003, Purdue began distributing an OxyContin branded goniometer—a range and motion measurement guide. According to DEA, Purdue's use of branded promotional items to market OxyContin was unprecedented among schedule II opioids, and was an indicator of Purdue's aggressive and inappropriate marketing of OxyContin.

Another approach Purdue used to promote OxyContin was to place advertisements in medical journals. Purdue's annual spending for OxyContin advertisements increased from about $700,000 in 1996 to about $4.6 million in 2001. All three companies that marketed the comparable drugs have also used medical journal advertisements to promote their products.

OxyContin Advertisements Violated the FD&C Act

Purdue has been cited twice by FDA for using advertisements in professional medical journals that violated the FD&C Act. In May 2000, FDA issued an untitled letter to Purdue regarding a professional medical

[35]It is common drug industry practice for companies to provide conversion tables for sales representatives to distribute to health care practitioners. Purdue used a similar pen for its older product, MS Contin.